133008

Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: S. Kumar Examiner #: 69544 Date: 9/26/01
Art Unit: 1621 Phone Number 30[illegible] 2-0640 Serial Number: 10/695536
Mail Box and Bldg/Room Location: [illegible] 5C03 Results Format Preferred (circle): PAPER DISK E-MAIL
5C18

If more than one search is submitted, please prioritize searches in order of need.

****

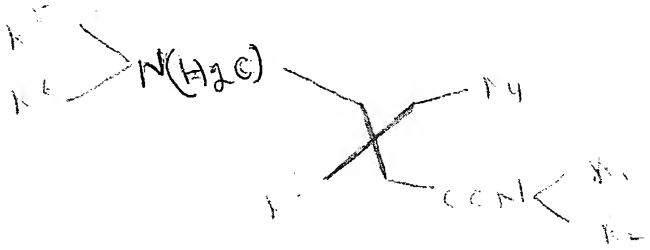
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

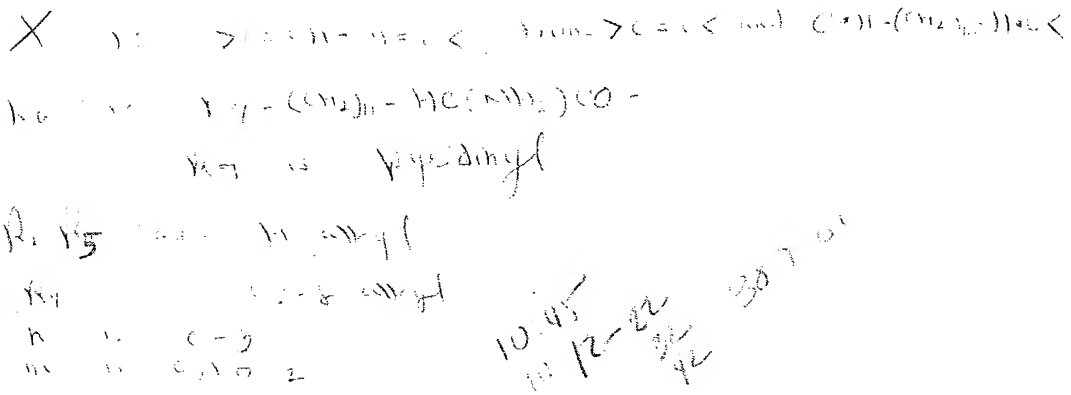
Title of Invention: Antagonists of the magnesium binding defect as therapeutic

Inventors (please provide full names): Ilert Clifton Wells

Earliest Priority Filing Date: 8/9/2000

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*





See claims.

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STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
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Date Searcher Picked Up:	Bibliographic		Dr.Link	
Date Completed: 9/27	Litigation		Lexis/Nexis	
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PTO-1590 (8-01)

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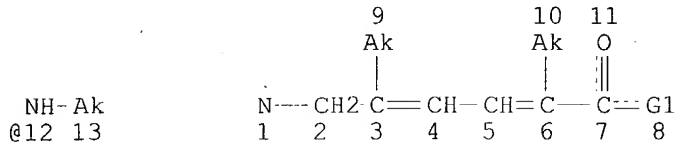

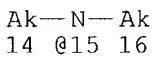

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STEREO ATTRIBUTES: NONE
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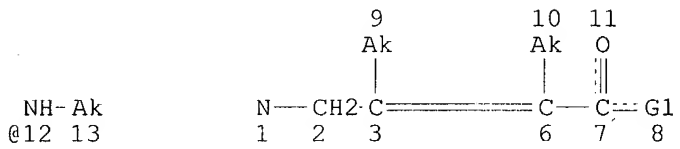

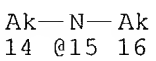

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STEREO ATTRIBUTES: NONE
L7 4 SEA FILE=REGISTRY SSS FUL L1 OR L3

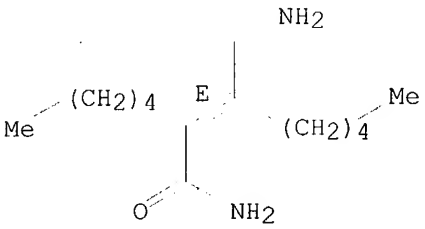
100.0% PROCESSED 19305 ITERATIONS 4 ANSWERS
SEARCH TIME: 00.00.01

L7 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2004 ACS on STN
RN 398125-90-1 REGISTRY

Searched by: Mary Hale 571-272-2507 REM 1D86

CN 2-Octenamide, 3-(aminomethyl)-2-pentyl-, (2E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C14 H28 N2 O
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:161401 Antagonists of the magnesium binding defect as therapeutic agents and methods for treatment of abnormal physiological states. Wells, Ibert Clifton (Magnesium Diagnostics, Inc., USA). PCT Int. Appl. WO 2002011714 A2 20020214, 38 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US24909 20010809. PRIORITY: US 2000-635266 20000809.

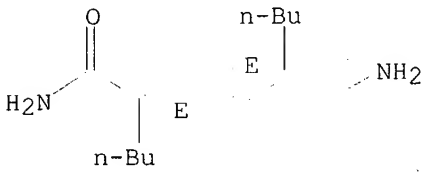
AB This invention provides a class of therapeutic compds. and methods for the treatment of mammals with physiol. disorders, for example, a frequently occurring type of essential hypertension, which are critically associated with the decreased binding of magnesium to the plasma membranes of their cells, insulin resistance of type 2 diabetes mellitus, and pre-eclampsia/eclampsia. These methods consist of administering to a mammal in need of such treatment a compound selected from a series of disubstituted trans,trans-1,3-butadienes, 1,3-disubstituted perhydrobutadienes, 1,2-disubstituted trans-ethylenes, 1,2-disubstituted ethanes, and disubstituted propanes, each of which embodies, in common, the unique structural feature essential for the biol. activity of these compds. This invention also provides for pharmaceutical formulations that employ these novel compds. For example, N-(2,4-di-n-amylpentanoic acid amide)-L-phenylglycinamide was prepared using diethylglutaric acid and n-amyl bromide as the starting compds.

L7 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2004 ACS on STN
RN 398125-82-1 REGISTRY
CN 2,4-Nonadienamide, 5-(aminomethyl)-2-butyl-, (2E,4E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C14 H26 N2 O
SR CA

Searched by: Mary Hale 571-272-2507 REM 1D86

LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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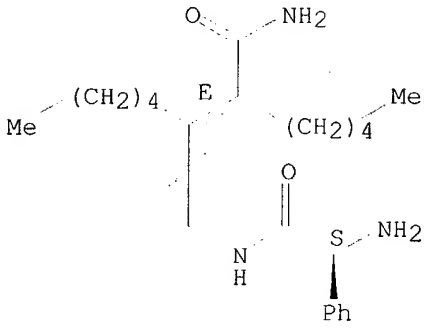
L7 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2004 ACS on STN
RN 398125-75-2 REGISTRY
CN Benzeneacetamide, α-amino-N-[(2E)-3-(aminocarbonyl)-2-pentyl-2-octenyl]-, (αS)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C22 H35 N3 O2
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

Searched by: Mary Hale 571-272-2507 REM 1D86

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

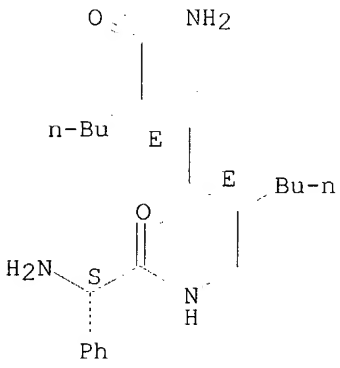
REFERENCE 1: 136:161401 Antagonists of the magnesium binding defect as therapeutic agents and methods for treatment of abnormal physiological states. Wells, Ibert Clifton (Magnesium Diagnostics, Inc., USA). PCT Int. Appl. WO 2002011714 A2 20020214, 38 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US24909 20010809. PRIORITY: US 2000-635266 20000809.

AB This invention provides a class of therapeutic compds. and methods for the treatment of mammals with physiol. disorders, for example, a frequently occurring type of essential hypertension, which are critically associated with the decreased binding of magnesium to the plasma membranes of their cells, insulin resistance of type 2 diabetes mellitus, and pre-eclampsia/eclampsia. These methods consist of administering to a mammal in need of such treatment a compound selected from a series of disubstituted trans,trans-1,3-butadienes, 1,3-disubstituted perhydrobutadienes, 1,2-disubstituted trans-ethylenes, 1,2-disubstituted ethanes, and disubstituted propanes, each of which embodies, in common, the unique structural feature essential for the biol. activity of these compds. This invention also provides for pharmaceutical formulations that employ these novel compds. For example, N-(2,4-di-n-amylpentanoic acid amide)-L-phenylglycinamide was prepared using diethylglutaric acid and n-amyl bromide as the starting compds.

L7 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2004 ACS on STN
RN 398125-74-1 REGISTRY
CN Benzeneacetamide, α-amino-N-[(2E,4E)-5-(aminocarbonyl)-2-butyl-2,4-nonadienyl]-, (αS)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C22 H33 N3 O2
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Searched by: Mary Hale 571-272-2507 REM 1D86

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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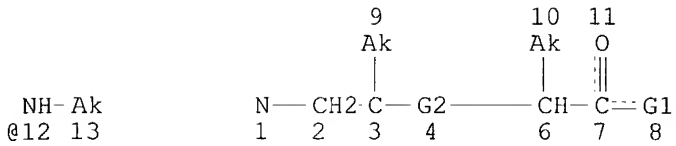
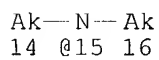
Searched by: Mary Hale 571-272-2507 REM 1D86





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DEFAULT ECLEVEL IS LIMITED

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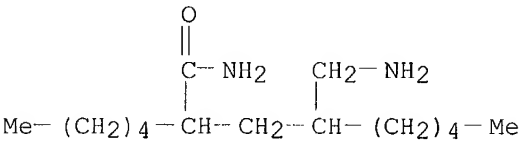
STEREO ATTRIBUTES: NONE
L8 SCR 1838
L10 11 SEA FILE=REGISTRY SSS FUL L4 NOT L8

100.0% PROCESSED 138849 ITERATIONS 11 ANSWERS
SEARCH TIME: 00.00.09

L10 ANSWER 1 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN 398125-96-7 REGISTRY
CN Nonanamide, 4-(aminomethyl)-2-pentyl-, monohydrochloride (9CI) (CA INDEX NAME)
MF C15 H32 N2 O . Cl H
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)



● HCl

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:161401 Antagonists of the magnesium binding defect as

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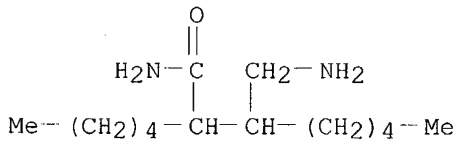
therapeutic agents and methods for treatment of abnormal physiological states. Wells, Ibert Clifton (Magnesium Diagnostics, Inc., USA). PCT Int. Appl. WO 2002011714 A2 20020214, 38 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US24909 20010809. PRIORITY: US 2000-635266 20000809.

AB This invention provides a class of therapeutic compds. and methods for the treatment of mammals with physiol. disorders, for example, a frequently occurring type of essential hypertension, which are critically associated with the decreased binding of magnesium to the plasma membranes of their cells, insulin resistance of type 2 diabetes mellitus, and pre-eclampsia/eclampsia. These methods consist of administering to a mammal in need of such treatment a compound selected from a series of disubstituted trans,trans-1,3-butadienes, 1,3-disubstituted perhydrobutadienes, 1,2-disubstituted trans-ethylenes, 1,2-disubstituted ethanes, and disubstituted propanes, each of which embodies, in common, the unique structural feature essential for the biol. activity of these compds. This invention also provides for pharmaceutical formulations that employ these novel compds. For example, N-(2,4-di-n-amylpentanoic acid amide)-L-phenylglycinamide was prepared using diethylglutaric acid and n-amyl bromide as the starting compds.

L10 ANSWER 2 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN 398125-91-2 REGISTRY
CN Octanamide, 3-(aminomethyl)-2-pentyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C14 H30 N2 O
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)



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Searched by: Mary Hale 571-272-2507 REM 1D86

GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US24909 20010809. PRIORITY: US 2000-635266 20000809.

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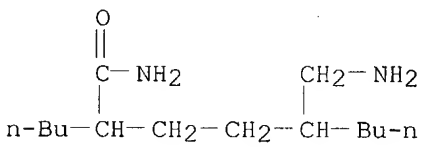
L10 ANSWER 3 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN 398125-84-3 REGISTRY
CN Nonanamide, 5-(aminomethyl)-2-butyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C14 H30 N2 O
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:161401 Antagonists of the magnesium binding defect as therapeutic agents and methods for treatment of abnormal physiological states. Wells, Ibert Clifton (Magnesium Diagnostics, Inc., USA). PCT Int. Appl. WO 2002011714 A2 20020214, 38 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US24909 20010809. PRIORITY: US 2000-635266 20000809.

AB This invention provides a class of therapeutic compds. and methods for the treatment of mammals with physiol. disorders, for example, a frequently occurring type of essential hypertension, which are critically associated with the decreased binding of magnesium to the plasma membranes of their cells, insulin resistance of type 2 diabetes mellitus, and pre-eclampsia/eclampsia. These methods consist of administering to a

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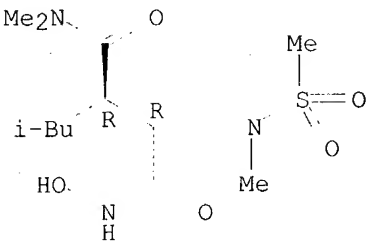
mammal in need of such treatment a compound selected from a series of disubstituted trans,trans-1,3-butadienes, 1,3-disubstituted perhydrobutadienes, 1,2-disubstituted trans-ethylenes, 1,2-disubstituted ethanes, and disubstituted propanes, each of which embodies, in common, the unique structural feature essential for the biol. activity of these compds. This invention also provides for pharmaceutical formulations that employ these novel compds. For example, N-(2,4-di-n-amylpentanoic acid amide)-L-phenylglycinamide was prepared using diethylglutaric acid and n-amyl bromide as the starting compds.

L10 ANSWER 4 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN 252562-65-5 REGISTRY
CN Butanediamide, N1-hydroxy-N4,N4-dimethyl-2-[[methyl(methylsulfonyl)amino]methyl]-3-(2-methylpropyl)-, (2R,3R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C13 H27 N3 O5 S
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

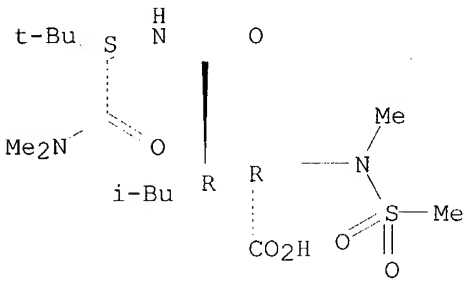
REFERENCE 1: 132:30315 The synthesis and biological evaluation of non-peptidic matrix metalloproteinase inhibitors. Martin, Fionna M.; Beckett, R. Paul; Bellamy, Claire L.; Courtney, Paul F.; Davies, Stephen J.; Drummond, Alan H.; Dodd, Rory; Pratt, Lisa M.; Patel, Sanjay R.; Ricketts, Michelle L.; Todd, Richard S.; Tuffnell, Andrew R.; Ward, John W. S.; Whittaker, Mark (British Biotech Pharmaceuticals Limited, Oxford, OX4 5LY, UK). Bioorganic & Medicinal Chemistry Letters, 9(19), 2887-2892 (English) 1999. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier Science Ltd..
AB Novel sulfonamide matrix metalloproteinase inhibitors most with piperidine amide were synthesized by a route involving a stereoselective conjugate addition reaction. Enzyme selectivity was dependent on the nature of the sulfonamide substituents. Several compds. are potent selective collagenase inhibitors with good oral bioavailability.

L10 ANSWER 5 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN 220127-48-0 REGISTRY
CN Hexanoic acid, 3-[[[(1S)-1-[(dimethylamino)carbonyl]-2,2-dimethylpropyl]amino]carbonyl]-5-methyl-2-[[methyl(methylsulfonyl)amino]methyl]-, (2R,3R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH

Searched by: Mary Hale 571-272-2507 REM 1D86

MF C19 H37 N3 O6 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.

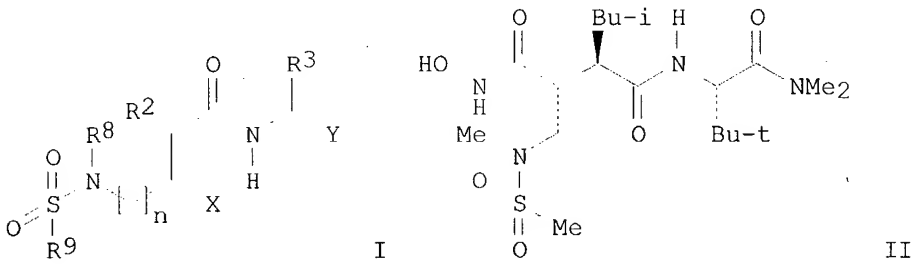


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 130:139082 Preparation of substituted succinamides as metalloproteinase inhibitors. Beckett, Raymond Paul; Martin, Fionna Mitchell; Miller, Andrew; Todd, Richard Simon; Whittaker, Mark (British Biotech Pharmaceuticals Limited, UK). PCT Int. Appl. WO 9903826 A2 19990128, 65 pp. DESIGNATED STATES: W: AU, BR, CA, CN, CZ, DE, GB, GE, HU, IL, JP, KR, MX, NO, NZ, PL, RU, SG, SK, TR, UA, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-GB2092 19980716. PRIORITY: GB 1997-15030 19970718.

GI



AB The title compds. [I; X = CO2H, CONHOH; n = 1-4; R2 = C1-12 alkyl, C2-12 alkenyl, C2-12 alkynyl, etc.; R3 = characterizing group of a natural or non-natural α amino acid in which any functional groups may be protected; R8 = H, C1-6 alkyl, PhCH2, etc.; R9 = (un)substituted C1-6 alkyl, cycloalkyl, cycloalkenyl, etc.; R8R9 = (un)substituted divalent C3-6 alkylene, alkenylene which may be fused to a Ph or heteroaryl; Y = C(O)NR4R5 (wherein R4 = (un)substituted cycloalkyl, cycloalkenyl, Ph, etc.; R5 = H, C1-6 alkyl), C(OH)R6R7 (R6 = H, C1-6 alkyl, phenyl(C1-6 alkyl), etc.; R7 = H, C1-6 alkyl; R6R7 together with carbon atoms to which they are attached form 5-6 membered carbocyclic or heterocyclic ring)], useful as matrix metalloproteinase inhibitors (no data), were prepared Thus, a multi-step synthesis of II, starting with 2-benzyloxycarbonyl-3R-

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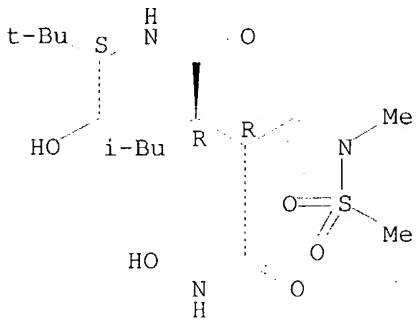
carboxy-5-methylhexanoic acid 1-benzyl ester 4-tert-Bu ester, was given. Compds. I are effective at 0.1-3 mg/kg/day.

L10 ANSWER 6 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN 220127-35-5 REGISTRY
CN Butanediamide, N1-hydroxy-N4-[(1S)-1-(hydroxymethyl)-2,2-dimethylpropyl]-2-[[methyl(methylsulfonyl)amino]methyl]-3-(2-methylpropyl)-, (2R,3R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C17 H35 N3 O6 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 130:139082 Preparation of substituted succinamides as metalloproteinase inhibitors. Beckett, Raymond Paul; Martin, Fionna Mitchell; Miller, Andrew; Todd, Richard Simon; Whittaker, Mark (British Biotech Pharmaceuticals Limited, UK). PCT Int. Appl. WO 9903826 A2 19990128, 65 pp. DESIGNATED STATES: W: AU, BR, CA, CN, CZ, DE, GB, GE, HU, IL, JP, KR, MX, NO, NZ, PL, RU, SG, SK, TR, UA, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-GB2092 19980716. PRIORITY: GB 1997-15030 19970718.

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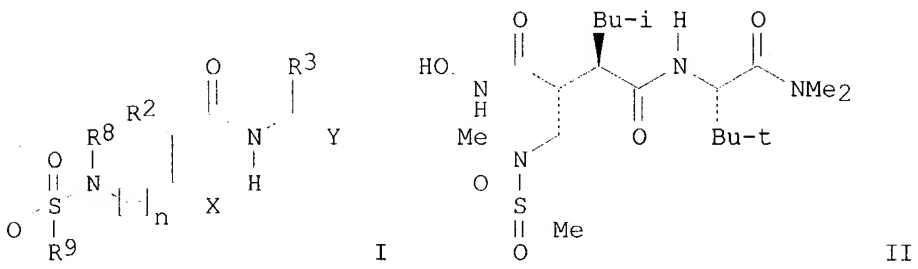
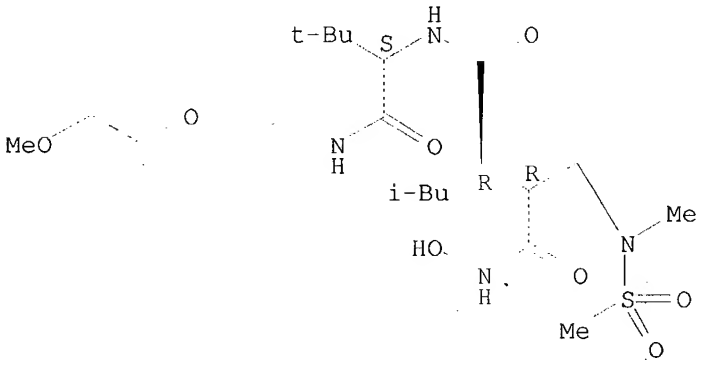


Searched by: Mary Hale 571-272-2507 REM 1D86

AB The title compds. [I; X = CO2H, CONHOH; n = 1-4; R2 = C1-12 alkyl, C2-12 alkenyl, C2-12 alkynyl, etc.; R3 = characterizing group of a natural or non-natural α amino acid in which any functional groups may be protected; R8 = H, C1-6 alkyl, PhCH2, etc.; R9 = (un)substituted C1-6 alkyl, cycloalkyl, cycloalkenyl, etc.; R8R9 = (un)substituted divalent C3-6 alkylene, alkenylene which may be fused to a Ph or heteroaryl; Y = C(O)NR4R5 (wherein R4 = (un)substituted cycloalkyl, cycloalkenyl, Ph, etc.; R5 = H, C1-6 alkyl), C(OH)R6R7 (R6 = H, C1-6 alkyl, phenyl(C1-6 alkyl), etc.; R7 = H, C1-6 alkyl; R6R7 together with carbon atoms to which they are attached form 5-6 membered carbocyclic or heterocyclic ring)], useful as matrix metalloproteinase inhibitors (no data), were prepared Thus, a multi-step synthesis of II, starting with 2-benzyloxycarbonyl-3R-carboxy-5-methylhexanoic acid 1-benzyl ester 4-tert-Bu ester, was given. Compds. I are effective at 0.1-3 mg/kg/day.

L10 ANSWER 7 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN 220127-33-3 REGISTRY
CN Butanediamide, N1-hydroxy-N4-[(1S)-1-[[[2-(2-methoxyethoxy)ethyl]amino]carbonyl]-2,2-dimethylpropyl]-2-[[methyl(methylsulfonyl)amino]methyl]-3-(2-methylpropyl)-, (2R,3R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C22 H44 N4 O8 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 130:139082 Preparation of substituted succinamides as metalloproteinase inhibitors. Beckett, Raymond Paul; Martin, Fionna Mitchell; Miller, Andrew; Todd, Richard Simon; Whittaker, Mark (British Biotech Pharmaceuticals Limited, UK). PCT Int. Appl. WO 9903826 A2 19990128, 65 pp. DESIGNATED STATES: W: AU, BR, CA, CN, CZ, DE, GB, GE, HU, IL, JP, KR, MX, NO, NZ, PL, RU, SG, SK, TR, UA, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-GB2092 19980716. PRIORITY: GB 1997-15030 19970718.
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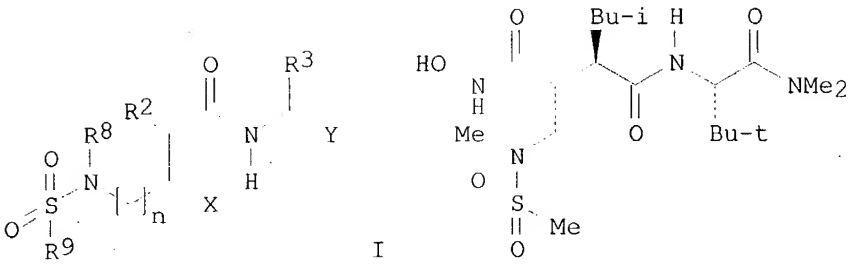
Searched by: Mary Hale 571-272-2507 REM 1D86



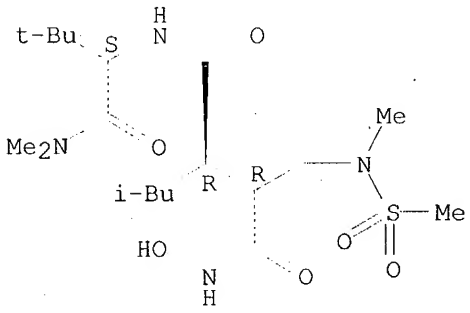
I

II

AB The title compds. [I; X = CO2H, CONHOH; n = 1-4; R2 = C1-12 alkyl, C2-12 alkenyl, C2-12 alkynyl, etc.; R3 = characterizing group of a natural or non-natural α amino acid in which any functional groups may be protected; R8 = H, C1-6 alkyl, PhCH2, etc.; R9 = (un)substituted C1-6 alkyl, cycloalkyl, cycloalkenyl, etc.; R8R9 = (un)substituted divalent C3-6 alkylene, alkenylene which may be fused to a Ph or heteroaryl; Y = C(O)NR4R5 (wherein R4 = (un)substituted cycloalkyl, cycloalkenyl, Ph, etc.; R5 = H, C1-6 alkyl), C(OH)R6R7 (R6 = H, C1-6 alkyl, phenyl(C1-6 alkyl), etc.; R7 = H, C1-6 alkyl; R6R7 together with carbon atoms to which they are attached form 5-6 membered carbocyclic or heterocyclic ring)], useful as matrix metalloproteinase inhibitors (no data), were prepared Thus, a multi-step synthesis of II, starting with 2-benzyloxycarbonyl-3R-carboxy-5-methylhexanoic acid 1-benzyl ester 4-tert-Bu ester, was given. Compds. I are effective at 0.1-3 mg/kg/day.

L10 ANSWER 8 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN 220127-32-2 REGISTRY
CN Butanediamide, N4-[(1S)-1-[(dimethylamino)carbonyl]-2,2-dimethylpropyl]-N1-hydroxy-2-[[methyl(methylsulfonyl)amino]methyl]-3-(2-methylpropyl)-, (2R,3R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H38 N4 O6 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

Searched by: Mary Hale 571-272-2507 REM 1D86

REFERENCE 1: 130:139082 Preparation of substituted succinamides as metalloproteinase inhibitors. Beckett, Raymond Paul; Martin, Fionna Mitchell; Miller, Andrew; Todd, Richard Simon; Whittaker, Mark (British Biotech Pharmaceuticals Limited, UK). PCT Int. Appl. WO 9903826 A2 19990128, 65 pp. DESIGNATED STATES: W: AU, BR, CA, CN, CZ, DE, GB, GE, HU, IL, JP, KR, MX, NO, NZ, PL, RU, SG, SK, TR, UA, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-GB2092 19980716. PRIORITY: GB 1997-15030 19970718.

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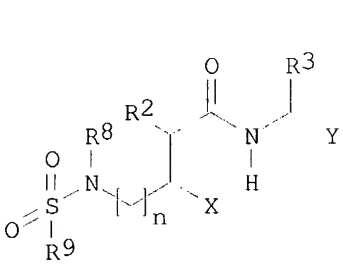
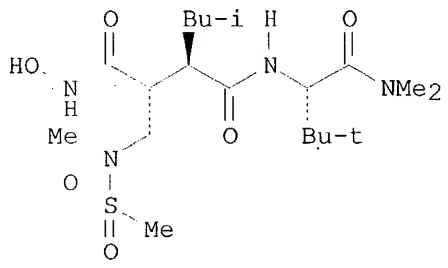


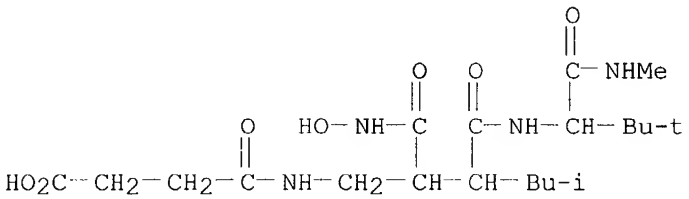
I



II

AB The title compds. [I; X = CO2H, CONHOH; n = 1-4; R2 = C1-12 alkyl, C2-12 alkenyl, C2-12 alkynyl, etc.; R3 = characterizing group of a natural or non-natural α amino acid in which any functional groups may be protected; R8 = H, C1-6 alkyl, PhCH2, etc.; R9 = (un)substituted C1-6 alkyl, cycloalkyl, cycloalkenyl, etc.; R8R9 = (un)substituted divalent C3-6 alkylene, alkenylene which may be fused to a Ph or heteroaryl; Y = C(O)NR4R5 (wherein R4 = (un)substituted cycloalkyl, cycloalkenyl, Ph, etc.; R5 = H, C1-6 alkyl), C(OH)R6R7 (R6 = H, C1-6 alkyl, phenyl(C1-6 alkyl), etc.; R7 = H, C1-6 alkyl; R6R7 together with carbon atoms to which they are attached form 5-6 membered carbocyclic or heterocyclic ring)], useful as matrix metalloproteinase inhibitors (no data), were prepared Thus, a multi-step synthesis of II, starting with 2-benzyloxycarbonyl-3R-carboxy-5-methylhexanoic acid 1-benzyl ester 4-tert-Bu ester, was given. Compds. I are effective at 0.1-3 mg/kg/day.

L10 ANSWER 9 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN 145339-07-7 REGISTRY
CN Butanoic acid, 4-[[3-[[[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]amino]carbonyl]-2-[(hydroxyamino)carbonyl]-5-methylhexyl]amino]-4-oxo- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H36 N4 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation)



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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 118:169601 Amino acid derivatives. Broadhurst, Michael John; Brown, Paul Anthony; Johnson, William Henry; Lawton, Geoffrey (Hoffmann-La Roche, F., und Co. A.-G., Switz.). Eur. Pat. Appl. EP 497192 A2 19920805, 65 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1992-100953 19920122. PRIORITY: GB 1991-2194 19910201; GB 1991-23162 19911031.

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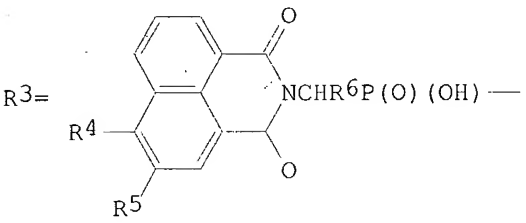
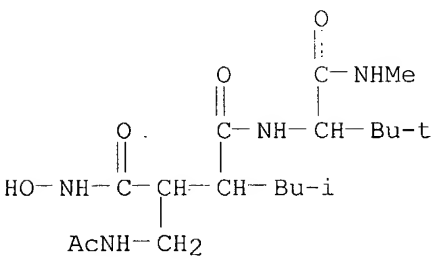


AB RCHR1CH(CH2CHMe2)CONHCH(CMe3)CONHR2 [I, R = CONHOH, R3; R1 = H, (un)substituted NH2, (un)substituted alkyl; R2 = H, (un)substituted alkyl; R4 = H, OH, alkoxy, OCH2Ph; R5 = H, halogen; R6 = H, alkyl, hydroxyalkyl, aminoalkyl] were prepared Thus, I (R = CONHOH, R1 = H, R2 = Me, II) was prepared from (R)-HO2CCH(CH2CHMe2)CH2CO2CMe3 and (S)-Me3CCH(NH2)CONHMe in 3 steps. II had a collagenase-inhibiting ED50 of 4 nM.

L10 ANSWER 10 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN 145339-02-2 REGISTRY
CN Butanediamide, 2-[(acetylamino)methyl]-N4-[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1-hydroxy-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H34 N4 O5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

Searched by: Mary Hale 571-272-2507 REM 1D86

REFERENCE 1: 118:169601 Amino acid derivatives. Broadhurst, Michael John; Brown, Paul Anthony; Johnson, William Henry; Lawton, Geoffrey (Hoffmann-La Roche, F., und Co. A.-G., Switz.). Eur. Pat. Appl. EP 497192 A2 19920805, 65 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1992-100953 19920122. PRIORITY: GB 1991-2194 19910201; GB 1991-23162 19911031.

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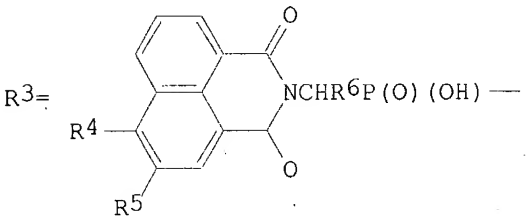
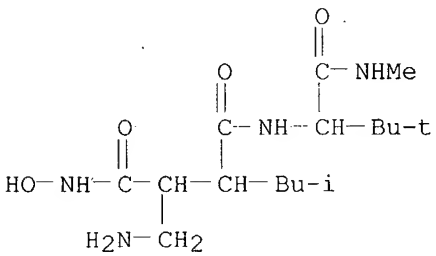


AB RCHR1CH(CH2CHMe2)CONHCH(CMe3)CONHR2 [I, R = CONHOH, R3; R1 = H, (un)substituted NH2, (un)substituted alkyl; R2 = H, (un)substituted alkyl; R4 = H, OH, alkoxy, OCH2Ph; R5 = H, halogen; R6 = H, alkyl, hydroxyalkyl, aminoalkyl] were prepared Thus, I (R = CONHOH, R1 = H, R2 = Me, II) was prepared from (R)-HO2CCH(CH2CHMe2)CH2CO2CMe3 and (S)-Me3CCH(NH2)CONHMe in 3 steps. II had a collagenase-inhibiting ED50 of 4 nM.

L10 ANSWER 11 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN 145339-00-0 REGISTRY
CN Butanediamide, 2-(aminomethyl)-N4-[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1-hydroxy-3-(2-methylpropyl)-, monohydrochloride (9CI) (CA INDEX NAME)
MF C16 H32 N4 O4 . Cl H
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation)



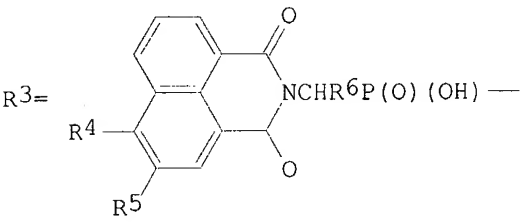
● HCl

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 118:169601 Amino acid derivatives. Broadhurst, Michael John; Brown, Paul Anthony; Johnson, William Henry; Lawton, Geoffrey (Hoffmann-La Roche, F., und Co. A.-G., Switz.). Eur. Pat. Appl. EP 497192 A2 19920805,

65 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1992-100953 19920122. PRIORITY: GB 1991-2194 19910201; GB 1991-23162 19911031.

GI



AB RCHR1CH(CH2CHMe2)CONHCH(CMe3)CONHR2 [I, R = CONHOH, R3; R1 = H, (un)substituted NH2, (un)substituted alkyl; R2 = H, (un)substituted alkyl; R4 = H, OH, alkoxy, OCH2Ph; R5 = H, halogen; R6 = H, alkyl, hydroxyalkyl, aminoalkyl] were prepared Thus, I (R = CONHOH, R1 = H, R2 = Me, II) was prepared from (R)-HO2CCH(CH2CHMe2)CH2CO2CMe3 and (S)-Me3CCH(NH2)CONHMe in 3 steps. II had a collagenase-inhibiting ED50 of 4 nM.

=> fil hcaplus;e magnesium binding/ct

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	461.49	848.50

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-9.90	-19.80

FILE 'HCAPLUS' ENTERED AT 10:40:42 ON 27 SEP 2004

FILE COVERS 1907 - 27 Sep 2004 VOL 141 ISS 14
FILE LAST UPDATED: 26 Sep 2004 (20040926/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

E#	FREQUENCY	AT	TERM
E1	0	4	MAGNESIUM ARSENATE HALIDE SULFATES/CT

Searched by: Mary Hale 571-272-2507 REM 1D86

```
E2            0      2     MAGNESIUM ATP/CT
E3            0        --> MAGNESIUM BINDING/CT
E4            0      2     MAGNESIUM BORATE FIBERS/CT
E5            0      7     MAGNESIUM BORIDE (MGB2)/CT
E6            0      8     MAGNESIUM BROMIDE/CT
E7            0      2     MAGNESIUM BROMIDE (MGBR2)/CT
E8            0     14     MAGNESIUM CARBONATE/CT
E9            0      2     MAGNESIUM CARBONATE (MGCO3)/CT
E10           0      2     MAGNESIUM CARBONATE FIBERS/CT
E11           0      2     MAGNESIUM CARBOXYLATES/CT
E12           1            MAGNESIUM CASEINATE/CT

=> s magnesium bind?
        410368 MAGNESIUM
            88 MAGNESIUMS
        410402 MAGNESIUM
                 (MAGNESIUM OR MAGNESIUMS)
       1064590 BIND?
L11        728 MAGNESIUM BIND?
                 (MAGNESIUM(W)BIND?)

=> s l11(l)(therap? or pharma? or treat?)
        385033 THERAP?
        503848 PHARMA?
       3086720 TREAT?
L12          6 L11(L)(THERAP? OR PHARMA? OR TREAT?)

=> d 1-6 cbib abs

L12  ANSWER 1 OF 6  HCAPLUS  COPYRIGHT 2004 ACS on STN
2004:594329  Emerging experimental therapeutics for bipolar disorder: insights
     from the molecular and cellular actions of current mood stabilizers.
     Gould, T. D.; Quiroz, J. A.; Singh, J.; Zarate, C. A., Jr.; Manji, H. K.
     (Laboratory of Molecular Pathophysiology, National Institute of Mental
     Health, Bethesda, MD, 20892, USA). Molecular Psychiatry, 9(8), 734-755
     (English) 2004. CODEN: MOPSFQ. ISSN: 1359-4184. Publisher: Nature
     Publishing Group.
AB   Bipolar disorder afflicts approx. 1-3% of both men and women, and is
     coincident with major economic, societal, medical, and interpersonal
     consequences. Current mediations used for its treatment are
     associated with variable rates of efficacy and often intolerable side
     effects. While preclin. and clin. knowledge in the neurosciences has
     expanded at a tremendous rate, recent years have seen no major
     breakthroughs in the development of novel types of treatment for
     bipolar disorder. We review here approaches to develop novel
     treatments specifically for bipolar disorder. Deliberate (ie not
     by serendipity) treatments may come from one of two general
     mechanisms: (1) Understanding the mechanism of action of current
     medications and thereafter designing novel drugs that mimics these
     mechanism(s); (2) Basing medication development upon the hypothetical or
     proven underlying pathophysiol. of bipolar disorder. In this review, we
     focus upon the first approach. Mol. and cellular targets of current mood
     stabilizers include lithium inhibitable enzymes where lithium competes for
     a magnesium binding site (inositol monophosphatase,
     inositol polyphosphate 1-phosphatase, glycogen synthase kinase-3 (GSK-3),
     fructose 1,6-bisphosphatase, bisphosphate nucleotidase,
     phosphoglucomutase), valproate inhibitable enzymes (succinate semialdehyde
     dehydrogenase, succinate semialdehyde reductase, histone deacetylase),
     targets of carbamazepine (sodium channels, adenosine receptors, adenylate
     cyclase), and signaling pathways regulated by multiple drugs of different
     classes (phosphoinositol/protein kinase C, cAMP, arachidonic acid,
     neurotrophic pathways). While the task of developing novel medications
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for bipolar disorder is truly daunting, we are hopeful that understanding the mechanism of action of current mood stabilizers will ultimately lead clin. trials with more specific medications and thus better **treatments** those who suffer from this devastating illness.

L12 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
2002:122777 Document No. 136:161401 Antagonists of the **magnesium binding** defect as **therapeutic** agents and methods for **treatment** of abnormal physiological states. Wells, Ibert Clifton (Magnesium Diagnostics, Inc., USA). PCT Int. Appl. WO 2002011714 A2 20020214, 38 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US24909 20010809. PRIORITY: US 2000-635266 20000809.
AB This invention provides a class of therapeutic compds. and methods for the treatment of mammals with physiol. disorders, for example, a frequently occurring type of essential hypertension, which are critically associated with the decreased binding of magnesium to the plasma membranes of their cells, insulin resistance of type 2 diabetes mellitus, and pre-eclampsia/eclampsia. These methods consist of administering to a mammal in need of such treatment a compound selected from a series of disubstituted trans,trans-1,3-butadienes, 1,3-disubstituted perhydrobutadienes, 1,2-disubstituted trans-ethylenes, 1,2-disubstituted ethanes, and disubstituted propanes, each of which embodies, in common, the unique structural feature essential for the biol. activity of these compds. This invention also provides for pharmaceutical formulations that employ these novel compds. For example, N-(2,4-di-n-amylpentanoic acid amide)-L-phenylglycinamide was prepared using diethylglutaric acid and n-amyl bromide as the starting compds.

L12 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
2001:549719 Document No. 136:273037 Neuroprotective and cognition-enhancing properties of MK-801 flexible analogs: Structure-activity relationships. Bachurin, Sergey; Tkachenko, Sergey; Baskin, Igor; Lermontova, Nadegda; Mukhina, Tatyana; Petrova, Lyudmila; Ustinov, Anatoliy; Proshin, Alexey; Grigoriev, Vladimir; Lukoyanov, Nikolay; Palyulin, Vladimir; Zefirov, Nikolay (Institute of Physiologically Active Compounds RAS, Chernogolovka, 142432, Russia). Annals of the New York Academy of Sciences, 939(Neuroprotective Agents), 219-236 (English) 2001. CODEN: ANYAA9. ISSN: 0077-8923. Publisher: New York Academy of Sciences.
AB Neuroprotective and biobehavioral properties of a series of novel open chain MK-801 analogs, as well as their structure-activity relationships have been investigated. Three groups of compds. were synthesized: monobenzylamino, benzhydrylamino, and dibenzylamino (DBA) analogs of MK-801. It was revealed that DBA analogs exhibit pronounced glutamate-induced calcium uptake blocking properties and anti-NMDA activity. The hit compound of DBA series, NT-1505, was investigated for its ability to improve cognition functions in animal model of Alzheimer's disease type dementia, simulated by **treating** animals with cholinotoxin AF64A. The results from an active avoidance test and a Morris water maze test showed that exptl. animals, **treated** addnl. with NT-1505, exhibited much better learning ability and memory than the control group (AF64A **treated**) and close to that of the vehicle group of animals (**treated** with physiol. solution). Study of NT-1505 influence on locomotor activity revealed that it is characterized by a spectrum of behavioral activity radically different from that of MK-801, and in contrast to the latter one does not produce

any psychotomimetic side effects in the **therapeutically** significant dose interval. The computed docking of MK-801 and its flexible analogs on the NMDA receptor elucidated the crucial role of the hydrogen bond formed between these compds. and the asparagine residue for **magnesium binding** in the NMDA receptor. It was suggested that strong hydrophobic interaction between MK-801 and the hydrophobic pocket in the NMDA receptor-channel complex dets. much higher irreversibility of this adduct compared to the intermediates formed between this site and Mg ions of flexible DBA derivs., which might explain the absence of PCP-like side effects of the latter compds.

L12 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
2001:207891 Document No. 134:244265 Radiation source for endovascular radiation treatment in form of a wire. Fritz, Eberhard; Menuhr, Helmut; Hunt, Dave (Aea Technology QSA G.m.b.H., Germany). Eur. Pat. Appl. EP 1084733 A1 20010321, 9 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 1999-118544 19990920.
AB The present invention relates to a radioactive radiation source as a wire comprising a matrix of a ductile and/or plastic binder material and a radioactive and/or activable material. Preferably the elastic binder material is a metal, a metal alloy or a radiation resistant plastic material or mixture thereof. The radioactive or then activated activable material is a β-emitter, a γ-emitter or x-ray emitter. The source may further comprise a means for containment. The radioactive radiation source of the invention is preferably used in intravascular radiation treatment e.g. to treat cancer, tumors, nonmalign cell growth, or scar tissue or to prevent restenosis.

L12 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
1994:672026 Document No. 121:272026 Effect of chronic lithium administration on contractility of jejunum and uterus and inhibition by lithium and magnesium. Hemmings, F. J.; Edbury, S. M.; Davie, R. J.; Birch, N. J. (School Health Sciences, University Wolverhampton, Wolverhampton, UK). Lithium, 5(3), 161-8 (English) 1994. CODEN: LITHER. ISSN: 0954-1381.
AB The **pharmacol.** effects of chronic lithium **treatment** of rats were investigated using smooth muscle prepns. from the jejunum and uterus. In the jejunum, tissue contraction was evoked by means of carbachol (CCh) and, in the uterus, by carbachol and the hormones oxytocin and angiotensin II. The degree of inhibition caused by lithium and magnesium was measured in both control and chronically **treated** animals. Chronic lithium **treatment** of rats did not significantly alter tissue sensitivity to administration of lithium to the buffer solution either for carbachol- or oxytocin-induced contractions. Chronic lithium **treatment** enhanced depression by lithium of angiotensin II contractions of the uterus. Chronic lithium **treatment** reduced the inhibitory effects of magnesium on tissue contraction suggesting that lithium may interfere with **magnesium binding** on the G-protein sites or may compete for and inactivate magnesium-dependent enzymes.

L12 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
1981:543665 Document No. 95:143665 Amphotericin B binding of magnesium: contribution to its toxicity, and therapeutic implications. Seelig, Mildred S. (Goldwater Mem. Hosp. New York, Univ. Med. Cent., New York, NY, 10044, USA). Magnesium-Bulletin, 3(1), 80-4 (English) 1981. CODEN: MABUDW. ISSN: 0172-908X.
GI

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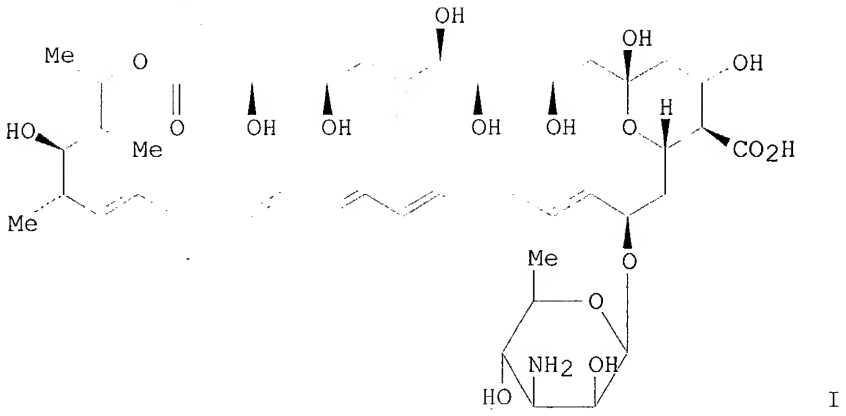

I

AB A review and discussion with 67 refs. on the effect of amphotericin B (I) [1397-89-3] binding to Mg on the toxicity and therapeutic effectiveness of I.

=> fil medl,biosis,embase;s magnesium bind? and (therap? or treat? or effect? or pharmac?)

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	22.38	870.88

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-4.20	-24.00

FILE 'MEDLINE' ENTERED AT 10:42:41 ON 27 SEP 2004

FILE 'BIOSIS' ENTERED AT 10:42:41 ON 27 SEP 2004
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FILE 'EMBASE' ENTERED AT 10:42:41 ON 27 SEP 2004
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L13 84 FILE MEDLINE
L14 99 FILE BIOSIS
L15 46 FILE EMBASE

TOTAL FOR ALL FILES
L16 229 MAGNESIUM BIND? AND (THERAP? OR TREAT? OR EFFECT? OR PHARMAC?)

=> s l16 and antagonist
L17 7 FILE MEDLINE
L18 3 FILE BIOSIS
L19 1 FILE EMBASE

TOTAL FOR ALL FILES
L20 11 L16 AND ANTAGONIST

=> dup rem l20
PROCESSING COMPLETED FOR L20
L21 9 DUP REM L20 (2 DUPLICATES REMOVED)

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=> d 1-9 cbib abs

L21 ANSWER 1 OF 9 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
2004:68194 Document No.: PREV200400068721. **Antagonists** of the **magnesium binding** defect as **therapeutic** agents and methods for **treatment** of abnormal physiological states. Wells, Ibert Clifton [Inventor, Reprint Author]. ASSIGNEE: Magnesium Diagnostics, Inc.. Patent Info.: US 6664420 December 16, 2003. Official Gazette of the United States Patent and Trademark Office Patents, (Dec 16 2003) Vol. 1277, No. 3. http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133 (ISSN print). Language: English.

AB This invention provides a class of **therapeutic** compounds and methods for the **treatment** of mammals with physiological disorders, such as for example a frequently occurring type of essential hypertension, which are critically associated with the decreased binding of magnesium to the plasma membranes of their cells. These methods consist of administering to a mammal in need of such **treatment** a compound selected from a series of disubstituted trans, trans 1,3-butadienes, 1,3-disubstituted perhydrobutadienes, 1,2-disubstituted trans ethylenes and 1,2 disubstituted ethanes and disubstituted propanes, each of which embodies, in common, the unique structural feature essential for the biological activity of these compounds. This invention also provides for **pharmaceutical** formulations that employ these novel compounds.

L21 ANSWER 2 OF 9 MEDLINE on STN
2003253826. PubMed ID: 12777712. Rat polymerase beta gapped DNA interactions: antagonistic **effects** of the 5' terminal PO4 - group and magnesium on the enzyme binding to the gapped DNAs with different ssDNA gaps. Jezewska Maria J; Galletto Roberto; Bujalowski Wlodzimierz. (Department of Human Biological Chemistry and Genetics, The University of Texas Medical Branch at Galveston, Galveston, TX 77555-1053, USA.) Cell biochemistry and biophysics, (2003) 38 (2) 125-60. Journal code: 9701934. ISSN: 1085-9195. Pub. country: United States. Language: English.

AB The role of the 5' terminal phosphate group downstream from the primer and magnesium cations in the energetics and dynamics of the gapped DNA recognition by rat polymerase beta have been examined, using the fluorescence titration and stopped-flow techniques. The analyses have been performed with the entire series of gapped DNA substrates differing in the size of the ssDNA gap. The 5' terminal phosphate group and magnesium cations exert antagonistic **effect** on enzyme binding to gapped DNA that depends on the length of the ssDNA gap. The PO4 - group amplifies the differences between the substrates with different ssDNA gaps, while in the presence of magnesium, affinities and structural changes induced in the DNA are very similar among examined DNA substrates. Both, the phosphate group and Mg+2 differ dramatically in affecting the thermodynamic response of the gapped DNA-rat pol beta system to the salt concentration. The data indicate that these distinct **effects** result from affecting the structure of the DNA, in the case of the phosphate group, and from direct **magnesium binding** to the protein. The mechanism of rat enzyme binding depends on the length of the ssDNA gap and the presence of the 5' terminal phosphate group. Complex formation with DNAs having three, four, and five residues in the gap occurs by a minimum three-step sequential mechanism. Depending on the presence of the 5' terminal phosphate group and/or **magnesium**, **binding** of the enzyme to a DNA containing two residues in the ssDNA gap is described by the same three-step or by a simpler two-step mechanism. With the DNA containing only one residue in the gap, binding is always described by only a two-step mechanism. The PO4 - group and magnesium cations have opposite **effects** on internal stability of

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the complexes with different length of the ssDNA gap. While the PO4 - group increases the stability of internal intermediates with the increasing length of the gap, Mg+2 decreases the stability of the intermediates with longer ssDNA gap. As a result, the combined favorable orientation **effect** of the phosphate group and the unfavorable Mg+2 **effect** lead to the optimal docking of the ssDNA gaps with three and four residues by the enzyme.

L21 ANSWER 3 OF 9 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
2002:596572 Document No.: PREV200200596572. **Antagonists** of the **magnesium binding** defect as **therapeutic** agents and methods for **treatment** of abnormal physiological states.
Wells, Ibert Clifton [Inventor, Reprint author]. Omaha, NE, USA. ASSIGNEE: Magnesium Diagnostics, Inc.. Patent Info.: US 6455734 September 24, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (Sep. 24, 2002) Vol. 1262, No. 4. http://www.uspto.gov/web/menu/patdata.html. e-file.
CODEN: OGUPE7. ISSN: 0098-1133. Language: English.
AB This invention provides a class of **therapeutic** compounds and methods for the **treatment** of mammals of physiological disorders, for example a frequently occurring type of essential hypertension, which are associated with the decreased binding of magnesium to the plasma membranes of their cells. These methods consist of administering to a mammal in need of such **treatment** a compound selected from a series of disubstituted trans,trans-1,3-butadienes, 1,3-perhydrobutadienes, 1,2-disubstituted trans ethylenes, and 1,2-disubstituted ethanes and disubstituted propanes, each of which embodies, in common, the unique structural feature essential for the biological activity of these compounds. This invention also provides for **pharmaceutical** formulations that employ these novel compounds.

L21 ANSWER 4 OF 9 MEDLINE on STN
2002190404. PubMed ID: 11923420. Glutamate but not glycine agonist affinity for NMDA receptors is influenced by small cations. Nahum-Levy Rinat; Tam Eyal; Shavit Sara; Benveniste Morris. (Department of Physiology and Pharmacology, Sackler School of Medicine, Tel Aviv University, Ramat Aviv, 69978 Israel.) Journal of neuroscience : official journal of the Society for Neuroscience, (2002 Apr 1) 22 (7) 2550-60. Journal code: 8102140. ISSN: 1529-2401. Pub. country: United States. Language: English.
AB NMDA receptor currents desensitize in an agonist-dependent manner when either the glutamate or glycine agonist is subsaturating. This may result from a conformational change in the NMDA receptor protein that lowers glutamate and glycine binding site affinity induced by co-agonist binding, channel opening, or ion permeation. We have used whole-cell voltage clamp of cultured hippocampal neurons with agonist paired-pulse protocols to demonstrate that glutamate and glycine dissociate 7.9- and 6.8-fold slower in the absence of their respective co-agonists than when their co-agonists are present. Paired-pulse and desensitization protocols were used to show that co-agonist binding and channel opening are sufficient to cause a reduction in glycine affinity, but extracellular sodium or **magnesium binding** was required in addition to conformational changes leading to channel opening to reduce glutamate binding-site affinity. Use of cesium or potassium as the major extracellular cation prevented the reduction of glutamate affinity. In addition, the use of choline-, sodium-, or cesium-based intracellular solutions did not alter desensitization characteristics, indicating that the site responsible for reduction of glutamate affinity is not in the intracellular domain. The fact that the reduction of glutamate affinity is dependent on certain small extracellular cations whereas the reduction of glycine affinity is insensitive to such cations indicates that conformational changes induced by the binding of glutamate are not completely paralleled by the conformational changes induced by glycine.

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Although glutamate and glycine are essential co-agonists, these data suggest that they have differential roles in the process of NMDA receptor activation.

L21 ANSWER 5 OF 9 MEDLINE on STN
2002072376. PubMed ID: 11798168. Glycogen synthase kinase-3 inhibition by lithium and beryllium suggests the presence of two **magnesium binding** sites. Ryves W Jonathan; Dajani Rana; Pearl Laurence; Harwood Adrian J. (MRC Laboratory for Molecular Cell Biology, University College London, Gower Street, London, WC1E 6BT, United Kingdom.) Biochemical and biophysical research communications, (2002 Jan 25) 290 (3) 967-72. Journal code: 0372516. ISSN: 0006-291X. Pub. country: United States. Language: English.

AB Lithium inhibits (Li(+)) glycogen synthase kinase-3 (GSK-3) by competition for magnesium (Mg(2+)), but not ATP or substrate. Here, we show that the group II metal ion beryllium (Be(2+)) is a potent inhibitor of GSK-3 and competes for both Mg(2+) and ATP. Be(2+) also inhibits the related protein kinase cdc2 at similar potency, but not MAP kinase 2. To compare the actions of Li(+) and Be(2+) on GSK-3, we have devised a novel dual inhibition analysis. When Be(2+) and ADP are present together each interferes with the action of the other, indicating that both agents inhibit GSK-3 at the ATP binding site. In contrast, Li(+) exerts no interference with ADP inhibition or vice versa. We find, however, that Li(+) and Be(2+) do interfere with each other. These results suggest that Be(2+) competes for two distinct Mg(2+) binding sites: one is Li(+)-sensitive and the other, which is Li(+)-insensitive, binds the Mg:ATP complex.

L21 ANSWER 6 OF 9 MEDLINE on STN
95081075. PubMed ID: 7989306. Shared active sites of fructose-1,6-bisphosphatase. Arginine 243 mediates substrate binding and fructose 2,6-bisphosphate inhibition. Giroux E; Williams M K; Kantrowitz E R. (Department of Chemistry, Merkert Chemistry Center, Boston College, Chestnut Hill, Massachusetts 02167.) Journal of biological chemistry, (1994 Dec 16) 269 (50) 31404-9. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB The active site of pig kidney fructose-1,6-bisphosphatase (EC 3.1.3.11) is shared between subunits, Arg-243 of one chain interacting with fructose-1,6-bisphosphate or fructose-2,6-bisphosphate in the active site of an adjacent chain. In this study, Arg-243 was replaced by alanine using techniques of site-specific mutagenesis and the cloned pig kidney enzyme expressed in Escherichia coli. Compared with wild-type enzyme, kinetic parameters of the altered enzyme characterizing catalytic efficiency, **magnesium binding**, and inhibition by AMP differed but by less than an order of magnitude; affinity for substrate fructose 1,6-bisphosphate was 10-fold poorer, and affinity for inhibitor fructose 2,6-bisphosphate was 1000-fold poorer. Molecular dynamics simulations were undertaken to determine possible alterations in active sites of the enzyme due to replacement of Arg-243 by Ala and suggested that in the mutant enzyme loss of one cationic group leads to reorganization of the active site especially involving lysine residues 269 and 274. The differences in properties of the mutant enzyme indicate the key importance of Arg-243 in the function of fructose-1,6-bisphosphatase and confirm on a functional basis the shared active site in this important metabolic enzyme.

L21 ANSWER 7 OF 9 MEDLINE on STN DUPLICATE 1
91042472. PubMed ID: 1978243. Competitive inhibition of magnesium-induced [3H]N-(1-[thienyl] cyclohexyl)piperidine binding by arcaine: evidence for a shared spermidine-**magnesium binding** site. Sacaan A I; Johnson K M. (Department of Pharmacology and Toxicology, University of Texas Medical Branch, Galveston 77550.) Molecular pharmacology, (1990

Searched by: Mary Hale 571-272-2507 REM 1D86

Nov) 38 (5) 705-10. Journal code: 0035623. ISSN: 0026-895X. Pub. country: United States. Language: English.

AB The polyamine competitive **antagonist** arcaine (1,4-diguanidino-butane) produced complete inhibition of basal [3H]N-(1-[thienyl] cyclohexyl)piperidine ([3H]TCP) binding, with an IC50 value of 4.52 +/- 0.93 microM. Arcaine (5 and 10 microM) produced a decrease in the affinity without a significant change in the receptor density of [3H]TCP binding under equilibrium conditions. In addition, arcaine did not alter either N-methyl-D-aspartate-specific [3H] glutamate or strychnine-insensitive [3H]glycine binding. Furthermore, increasing concentrations of arcaine produced parallel rightward shifts in the concentration-response curves for both spermidine- and magnesium-induced [3H]TCP binding, suggesting that arcaine is a competitive inhibitor of both agonists. Similar rightward shifts were observed for barium- and strontium-induced [3H]TCP binding. In contrast, arcaine decreased the efficacy of glutamate- and glycine-induced [3H]TCP binding without changing their EC50 values, indicating a noncompetitive type of inhibition. These results imply that spermidine and certain divalent cations including magnesium share the same mechanism for enhancing [3H]TCP binding, whereas glutamate and glycine have different sites of action. This is further supported by the additive **effect** of spermidine when tested in the presence of maximal concentrations of glutamate and glycine. On the other hand, spermidine and magnesium were not additive and, in fact, magnesium was able to block the **effects** of spermidine under certain conditions. The possibility that magnesium is a partial agonist at the polyamine site is discussed.

L21 ANSWER 8 OF 9 MEDLINE on STN

78190078. PubMed ID: 207492. Bactericidal action of ascorbic acid on Psuedomonas aeruginosa: alteration of cell surface as a possible mechanism. Rawal B D. Chemotherapy, (1978) 24 (3) 166-71. Journal code: 0144731. ISSN: 0009-3157. Pub. country: Switzerland. Language: English.

AB Neutralised ascorbic acid is found to exert a strong bactericidal action on Pseudomonas aeruginosa suspended in isotonic phosphate buffer at pH 7.1. Both the bactericidal and bacteriostatic action of ascorbic acid are antagonised by magnesium ions. In the absence of complex formation between magnesium and ascorbic acid it is concluded that ascorbic acid acts by competing with the **magnesium binding** sites in the cell wall, cell membrane or ribosomes. Using the chequer-board titration method the synergistic action of ascorbic acid and erythromycin is determined; such a potentiation of erythromycin is also adversely affected by magnesium ions. P. aeruginosa cells, washed and suspended in isotonic phosphate buffer containing ascorbic acid, became increasingly susceptible to the action of polymyxin, erythromycin, chloramphenicol, neomycin and tetracycline. It is suggested that ascorbic acid alters the cell surface to render it increasingly permeable to these antibiotics.

L21 ANSWER 9 OF 9 MEDLINE on STN

75114788. PubMed ID: 1167861. The control of adenylate cyclase by calcium in turkey erythrocyte ghosts. Steer M L; Levitzki A. Journal of biological chemistry, (1975 Mar 25) 250 (6) 2080-4. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB The adenylate cyclase of turkey erythrocytes is inhibited by low concentrations of calcium. Calcium binds to the enzyme system so tightly that the enzyme can compete with ethylene glycol bis(beta-aminoethyl ether)-N, N1-tetraacetic acid (EGTA) for the metal. The calcium binding site is shown to be distinct from the **magnesium binding** sites required for activity. Thus Ca2+ functions as a negative allosteric **effector**. Calcium decreases dramatically the V max of the catecholamine-stimulated activity without affecting the affinity for the hormone or for the substrate ATP. The cooperativity in the response toward Mg2+ dependence (Hill coefficient, nH equals 3) is also unaffected

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by Ca2+ where as the S0.5 (concentration yielding one-half V max) for Mg2+ is affected only slightly. The Ca2+ **effect** is cooperative (nH equals 2) and therefore brought about by a cluster of Ca2+ binding sites. Mn2+ can substitute for Mg2+ as the enzyme activator but the Mn2+-activated enzyme is no longer inhibited by Ca2+. The possible physiological significance of the Ca2+ **effect** is discussed.

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=> fil medl,hcapl,biosis,embase,wpids;s wells, i?/au,in or wells i?/au,in
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     8.19     879.07

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00     -24.00

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'IN' IS NOT A VALID FIELD CODE
L22          131 FILE MEDLINE
L23           96 FILE HCAPLUS
L24          118 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L25          112 FILE EMBASE
L26           21 FILE WPIDS

TOTAL FOR ALL FILES
L27          478 WELLS, I?/AU,IN OR WELLS I?/AU,IN

=> s l27 and magnesium(l)bind?(l)defect?
L28            3 FILE MEDLINE
L29            6 FILE HCAPLUS
L30            6 FILE BIOSIS
L31            3 FILE EMBASE
L32            3 FILE WPIDS

TOTAL FOR ALL FILES
L33           21 L27 AND MAGNESIUM(L) BIND?(L) DEFECT?

=> s l33 not l20
L34            3 FILE MEDLINE
L35            5 FILE HCAPLUS
L36            4 FILE BIOSIS
L37            3 FILE EMBASE
L38            2 FILE WPIDS


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TOTAL FOR ALL FILES
L39 17 L33 NOT L20

=> dup rem l39
PROCESSING COMPLETED FOR L39
L40 7 DUP REM L39 (10 DUPLICATES REMOVED)

=> d 1-7 cbib abs

L40 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
2004:722832 Document No. 141:221316 Methods for detecting deficient cellular membrane tightly bound magnesium for disease diagnoses. **Wells, Ibert C.** (USA). U.S. Pat. Appl. Publ. US 2004171093 A1 20040902, 21 pp., Cont.-in-part of U.S. Ser. No. 695,536. (English). CODEN: USXXCO. APPLICATION: US 2004-805881 20040322. PRIORITY: US 1999-265690 19990310; US 2000-635266 20000809; US 2002-53669 20020124; US 2002-230133 20020829; US 2003-695536 20031028.

AB This invention relates to methods for detecting the deficiency of **magnesium** tightly bound to plasma membranes of somatic cells, referred to as the **magnesium binding defect**. The invention also relates to methods for assessing certain abnormal physiol. states, such as, salt-sensitive essential hypertension, type 2 overt or prediabetes mellitus, and preeclampsia/eclampsia syndrome that are associated with the **magnesium binding defect** . The invention further relates to methods for generating **magnesium** deficient cell membranes and for identifying substances which promote **binding** of **magnesium** ions to the plasma membranes of somatic cells. Addnl., the invention relates to a **binding** pair members having affinity for the peptides and promoters of the invention.

L40 ANSWER 2 OF 7 MEDLINE on STN DUPLICATE 2
2004178350. PubMed ID: 15073408. Abnormal magnesium metabolism in etiology of salt-sensitive hypertension and type 2 diabetes mellitus. **Wells Ibert C;** Agrawal Devendra K; Anderson Robert J. (Department of Medicine, Creighton University School of Medicine, Omaha, NE 68178, USA.) Biological trace element research, (2004 May) 98 (2) 97-108. Journal code: 7911509. ISSN: 0163-4984. Pub. country: United States. Language: English.

AB A previously unknown genetic **defect** in **magnesium** metabolism (i.e., the **magnesium-binding defect** [MgBD]) was found to be associated with the cause of "salt-sensitive" essential hypertension in humans and rats. It inhibits the entrance of Mg2+ into the cell so that the intracellular concentrations of Mg2+ and MgATP2- are decreased. Consequently, the 300 enzyme reactions in the cell, especially the 100 that either use or produce MgATP2-, are inhibited. Thus, because the extrusion of intracellular Na+ requires MgATP2-, hypertension results when the involved MgATP2- requiring enzyme is inhibited. The MgBD is corrected by the tachykinin substance P, which occurs in normal blood plasma, and by the pentapeptide and its contained tetrapeptide, which are released from the C-terminal region of substance P by plasma aminopeptidases. In vivo, the intravenous administration of the tetrapeptide corrects the hypertension and the MgBD as well. The MgBD also occurs in type 2 diabetes mellitus and, thus, the decreased intracellular concentrations of Mg2+ and MgATP2- ions appear to be involved also in the cause of this disease, which is reputed to be the fifth most deadly disease in the world.

L40 ANSWER 3 OF 7 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
2002:293943 Document No.: PREV200200293943. Method for detecting deficient cellular membrane tightly bound magnesium for disease diagnoses. **Wells, Ibert C.** [Inventor, Reprint author]. Omaha, NE, USA.

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ASSIGNEE: Magnesium Diagnostics, Inc., Omaha, NE, USA. Patent Info.: US 6372440 April 16, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (Apr. 16, 2002) Vol. 1257, No. 3. http://www.uspto.gov/web/menu/patdata.html. e-file. CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

AB This invention relates to methods for detecting the deficiency of **magnesium** tightly bound to cellular membranes, i.e. **magnesium binding defect**, which deficiency is associated with certain abnormal physiological states e.g., salt-sensitive essential hypertension or Type 2 diabetes mellitus.

L40 ANSWER 4 OF 7 MEDLINE on STN DUPLICATE 3

2001553246. PubMed ID: 11599778. Coexisting independent sodium-sensitive and sodium-insensitive mechanisms of genetic hypertension in spontaneously hypertensive rats (SHR). **Wells I C;** Blotcky A J. (The Omaha Veterans Administration Medical Center, NE, USA.. brucew@magnolia-bronze.com) . Canadian journal of physiology and pharmacology, (2001 Sep) 79 (9) 779-84. Journal code: 0372712. ISSN: 0008-4212. Pub. country: Canada. Language: English.

AB Some essential hypertensive patients and genetic hypertensive rat strains have less than the normal levels of Mg2+ tightly bound to the plasma membranes of their erythrocytes and other cells, i.e., the **magnesium binding defect** (MgBD). This **binding defect** appears to cause increased passive permeability of the membrane to Na+ and thereby its increased intracellular concentration, particularly if the Na+-extrusion enzyme systems of the cell are also **defective**. The Na+-Ca2+ exchange system in the cell membrane exports Na+ and imports Ca2+, increasing the tone of the smooth muscle cell and thus producing hypertension (HTn). This HTn is Na+-sensitive. Evidence supporting this postulate was obtained by determining the intraerythrocyte total concentrations of Na+, Ca2+, K+, and Mg2+ in two strains of spontaneously hypertensive rats (SHR and SS/Jr rats, having the MgBD together with the other requisites of the Na+-sensitive pathway) and their respective controls (WKY and SR/Jr rats, in which this complete pathway is absent). The Na+ and Ca2+ concentrations in the hypertensive rats were increased, and that of K+ was decreased. The concentrations of these cations were very similar in the two hypertensive strains. The level of membrane tightly bound Ca2+ in SHR erythrocyte membranes was significantly higher than those in the other three rat strains, which were not statistically different from each other. These results support previously reported evidence of the existence of a novel HTn-generating mechanism in the SHR rat, in which the intracellular Ca2+ concentration is increased as the result of the enhanced diffusion of this ion into the cell and the accompanying deficiency of the Ca2+ extrusion enzyme systems. This pathway is therefore Na+-insensitive, i.e., Ca2+-sensitive.

L40 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4

2000:646243 Document No. 133:190228 Method for detecting deficient cellular membrane tightly bound magnesium for disease diagnoses. **Wells, Ibert C.** (USA). PCT Int. Appl. WO 2000054053 A1 20000914, 21 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US3707 20000309. PRIORITY: US 1999-265690 19990310.

AB This invention relates to methods for detecting the deficiency of **magnesium** tightly bound to cellular membranes, i.e.

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magnesium binding defect, which deficiency is associated with certain abnormal physiol. states, e.g., salt-sensitive essential hypertension or Type 2 diabetes mellitus.

L40 ANSWER 6 OF 7 MEDLINE on STN DUPLICATE 5

93153698. PubMed ID: 1493590. Abnormal magnesium metabolism in two rat models of genetic hypertension. **Wells I C**; Agrawal D K. (Department of Biomedical Sciences, Creighton University School of Medicine, Omaha, NB 68178.) Canadian journal of physiology and pharmacology, (1992 Sep) 70 (9) 1225-9. Journal code: 0372712. ISSN: 0008-4212. Pub. country: Canada. Language: English.

AB **Magnesium** concentrations in erythrocyte ghosts and arterial tissue of male, spontaneously hypertensive rats (SHR) were significantly less than in these tissues of male normotensive controls (Wistar-Kyoto; WKY) of the same age, which were also fed rat chow and tap water. The **magnesium** concentration in SHR erythrocyte ghosts was increased to the control value by incubating SHR erythrocytes with WKY blood plasma; SHR plasma did not affect the **magnesium** concentration in WKY erythrocyte ghosts. The **magnesium** concentrations in erythrocyte ghosts, aortas, and mesenteric arteries from female salt-sensitive (SS/JR) and salt-resistant (SR/JR) Dahl-derived rats, both maintained ad libitum on laboratory rat chow and either tap water or 0.9% NaCl, were not different but were significantly less than those of Sprague-Dawley rats considered as controls. While the ingestion of 0.9% NaCl had no effect on the **magnesium** concentrations measured in these animals, it caused the salt-sensitive rats to become severely hypertensive. It is evident from these observations that the decreased **binding** of **magnesium** to the plasma membrane of cells may be an inheritable metabolic **defect** that may be associated with the development of hypertension. However, in those instances of hypertension in which this **defect** occurs, it appears to be a contributing cause of the hypertension; by itself the **defect** is not a cause of hypertension.

L40 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

1992:649429 Document No. 117:249429 Abnormal magnesium metabolism in two rat models of genetic hypertension. **Wells, I. C.**; Agrawal, D. K. (Sch. Med., Creighton Univ., Omaha, NE, 68178, USA). Canadian Journal of Physiology and Pharmacology, 70(10), 1225-9 (English) 1992. CODEN: CJPPA3. ISSN: 0008-4212.

AB **Magnesium** concns. in erythrocyte ghosts and arterial tissue of male, spontaneously hypertensive rats (SHR) were significantly less than in these tissues of male normotensive controls (Wistar-Kyoto; WKY) of the same age, which were also fed rat chow and tap water. The **magnesium** concentration in SHR erythrocyte ghosts was increased to the control value by incubating SHR erythrocytes with WKY blood plasma; SHR plasma did not affect the **magnesium** concentration in WKY erythrocyte ghosts. The **magnesium** concns. in erythrocyte ghosts, aortas, and mesenteric arteries from female salt-sensitive (SS/JR) and salt-resistant (SR/JR) Dahl-derived rats, both maintained ad libitum on laboratory rat chow and either tap water or 0.9 % NaCl, were not different but were significantly less than those of Sprague-Dawley rats considered as controls. While the ingestion of 0.9% NaCl had no effect on the **magnesium** concns. measured in these animals, it caused the salt-sensitive rats to become severely hypertensive. It is evident from these observations that the decreased **binding** of **magnesium** to the plasma membrane of cells may be an inheritable metabolic **defect** that may be associated with the development of hypertension. However, in those instances of hypertension in which this **defect** occurs, it appears to be a contributing cause of the hypertension; by itself the **defect** is not a cause of hypertension.

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	19.00	898.07

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.10	-26.10

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